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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/981,239	10/18/2001	Rita De Santis	2818-64	6035

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EXAMINER	
QIAN, CELINE X	
ART UNIT	PAPER NUMBER
1636	5

DATE MAILED: 04/23/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/981,239	DE SANTIS, RITA	
	Examiner	Art Unit	
	Celine Qian	1636	

-- The MAILING DATE of this communication app ars on the cover sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 March 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *19-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-31 are pending in the application.

Election/Restrictions

Applicant's election with traverse of Group I (claims 1-18) in Paper No. 4 is acknowledged. The traversal is on the ground(s) that Groups I, II, IV, V and VI have same classification. Applicants further argue that the method of Group II and V can only be practiced with the cell of Group I. In addition, Applicants argue that the subject matter of Groups II, IV and VI are not patentably distinct from Groups I, II and V for similar reasons. The Examiner agrees that the inventions of Group II and V can only be practiced with the cell of Group I, however, the arguments are not found persuasive for the following reason:

Inventions I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, by applicant's admission, the cell of Group I can be used in the method of Group II and V, therefore, the inventions of Group I are patentably distinct from the invention of Group II. Similarly, the inventions of Group V are patentably distinct from the invention of Group I. Similar reason also apply to the subject matter of Groups I, II, V and Groups II, IV and VI.

Accordingly, claims 19-31 are withdrawn from consideration as being directed to a non-elected subject matter. Claim 1-18 are currently under consideration.

The requirement is still deemed proper and is therefore made FINAL.

Specification

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to **a single paragraph** on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and **legal phraseology** often used in patent claims, such as "means" and "**said**," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

The abstract of the disclosure is objected to because it contains more than one paragraph and legal phraseology "said" is used. Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-18 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for generating antigen presenting cells (APC) expressing MAGE1-4, NY-ESO-1, GAGE1-6 and SSX-2; wherein the APC is generated from tumor patient peripheral blood mononuclear cells (PMBC), does not reasonably provide enablement for a method of generating APC expressing any other tumor associated antigens (TAA), wherein the APC is generated from cells from healthy subject. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The nature of the invention is a method for generating APC cells expressing TAA by treating APC with hypomethylating agent. The specification discloses a method for generating APC cells expressing TAA belong to cancer-testis antigen (CTA) family by treating cells derived from PBMC of cancer patients with advanced stage of disease or healthy individual, with demethylating agent 5-aza-2-deoxcytidine (see examples 1-6).

The breath of the claims are very broad. The claims encompass a method for generating APC from any cell expressing any type of TAA by treating activated APC with hypomethylating agents. However, the guidance in the specification is limited. The specification only discloses that the APC (from peripheral blood mononuclear cells) expressing a limited number of TAAs which all belong to the CTA subfamily. The specification fails to disclose that whether the cells expressing tumor antigen are from healthy individual or cancer patients. The specification also fails to disclose other members of CTA family or other families of TAAs are induced by said method.

The state of art at the time of filing teaches there are a number of TAAs associated with human cancer (see Moigeon, 2001,Vaccine, 19: 1305-1326, table 3), including CTAs, mutated antigens, overexpressed antigens. Some of them are expressed by a variety of tumors (such as CTAs), whereas others are tumor specific (e.g. Mum1 and Caspase 8). Although the mechanism for all TAA expression is not completely understood at present, several pathways have been proposed and it appears that different mechanisms might be involved. For example, the activation of some members of the CTA family such as MAGE antigens have been associated with global hypomethylation in tumor cells (see page 1311, bridging paragraph of col.1 and 2). On the other hand, Moingeon also teach that TAAs can be expressed following activation of a

cryptic promoter within intronic sequence (e.g. NA 17-A in melanoma), pseudogene processing (e.g. melanoma NA 88-A) or frameshift mutation resulting in the utilization of alternative open reading frames (e.g. colon carcinoma associated antigens). In addition, TAAs also include carbohydrates, gangliosides, glyco lipids and mucins. Moreover, there are seven subfamilies within CTA family, each includes multiple genes (see Kirkin et al. 2002, Cancer Investigation, 20 (2): 222-236). At present, the mechanism for tumor specific expression of these genes is not known (see page 230, col. 2, 2nd paragraph, lines 1-2) except for MAGE, GAGE and LAGE, which are activated in tumor cells treated with 5-aza-2-deoxycytidine. However, the same treatment of normal diploid cells do not up-regulate the expression of MAGE1 gene (see page 230, Col.2, 2nd paragraph, line 7-9). Kirkin et al. point out that existing data on the induction of MAGE expression in normal cells are contradictory and further investigation is needed (see page 230-231, bridging paragraph). The specification does not teach that treating APC cells with 5-aza-2-deoxycytidine would induce any TAA expression. The specification only teaches a limited number of TAAs, which all belong to CTA family, that are induced by 5-aa-2-deoxycytidine treatment. The specification also fails to teach whether these TAA expressing cells are generated from patients with advanced disease or normal individual. Therefore, the activation of any tumor-associated antigen in APC by hypomethylating agents is unpredictable. The induction of any TAA, including those shown in the specification, in APC cells derived from normal individual by hypomethylating agent is also unpredictable.

Due to the lack of guidance from the specification and prior art, one skilled in the art would have to engage in undue amount of experimentation to practice the claimed invention commensurate in scope with these claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8, 15 and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 8, the term "shared not immunodominant cancer antigens" renders the claim indefinite because it is not clear what kind of cancer antigens applicants are referring to. In other words, it is not clear that if these antigens are not immunodominant, not cancer antigens, or their expression not shared by different tumors. As such, the metes and bounds of the claim cannot be established.

Regarding claim 15, the word "fibroblasts" appears twice in the claim. It is unclear if the first "fibroblasts" is different from the second "fibroblasts."

Claim 16 recites the limitation "histone deacetylase inhibitor" in line 1. However, step d) in claim 1 does not recite this term. There is insufficient antecedent basis for this limitation in the claim. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian whose telephone number is 703-306-0283. The examiner can normally be reached on 9:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Celine Qian, Ph.D.
April 22, 2002

REMY YUCEL, PH.D
SUPERVISORY PATENT EXAMINER
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